PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32676	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/10543	International filing date *(day/month/year)* 22.09.2003	Priority date *(day/month/year)* 23.09.2002
International Patent Classification (IPC) or both national classification and IPC C07D257/04		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02.04.2004	07.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Bérillon, L Telephone No. +49 89 2399-7078

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10543

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-36 as originally filed

Claims, Numbers

1-10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Statement

Novelty (N)	Yes:	Claims	1-7, 9
	No:	Claims	8,10
Inventive step (IS)	Yes:	Claims	1-7,9
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

1 Prior art

Reference is made to the following documents:

D1: EP-A-0 443 983
D2: US-A-5 468 867
D3: J. MED. CHEM., 1999, vol. 42, pages 3919-3933

2 Novelty

2.1 D1 discloses one compound which fall within the scope of present claim 8 (see title compound of example 55 a) on page 35 and is therefore prejudicial to the novelty of present claim 8. D1 equally discloses the acylation of said compound with valeroylchloride (see 55 b) on page 35 and is therefore prejudicial to the novelty of present claim 10.

2.2 Novelty is not affected by D2-D3 which disclose neither the process claimed in claims 1-7 and 10 nor the intermediates claimed in claims 8 or 9.

3 Inventive step

3.1 The present application relates to a process and intermediates thereof for the preparation of Valsartan consisting of the following steps:
step a): IIa + IIb □ IIc
step b): IIc + IId □ IIe
step c): IIe □ I
Step a) consists in reacting aldehyde IIa with chiral amine IIb using reductive amination conditions with or without in-situ reduction of the formed imine (compare claim 1 and claim 4). Closest prior art D1 discloses a similar preparation which differ however in that it uses the corresponding benzyl bromide of aldehyde IIa as starting material. Said benzyl bromide is displaced with a chiral amine (see reaction 55a in D1, page 35). No hint can be found in the prior art which would indicate such modification to the skilled person. Inventive step is therefore acknowledged for step

a). Accordingly, claims 1-7 meet the requirements of Article 33(3) PCT.

3.2 Claims 8 and 9 relate to intermediates of the above mentioned process. Said intermediates in case they are novel (see item 2.1) are considered inventive in view of their contribution to the inventive step of the overall process.